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4. TITLE AND SUBTITLE

Final Report on "Sculpting Molecular Potentials to Design Optimized Materials: The Inverse Design of New Molecular Structures" (Agreement #W911NF0410243)

5a. CONTRACT NUMBER

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5b. GRANT NUMBER

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6. AUTHORS

David N. Beratan, Weitao Yang, Michael J. Therien, Koen Clays

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAMES AND ADDRESSES

Duke University
Office of Research Support
Duke University
Durham, NC 27705 -

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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14. ABSTRACT

The aim of this project was to develop inverse design methods capable of designing optimized molecular species and materials. The project involved the development of continuous, integer, and hybrid molecular optimization methods that allow the identification of optimal target species. A component of this project involves the synthesis and characterization of these candidate materials. The target property in this project is the nonlinear optical response of organic species. The outcome of this project was a suite of methods useful for the design and

15. SUBJECT TERMS

inverse design, nonlinear optics, optimization, molecular design, structure-function relations

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	15. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			David Beratan
UU	UU	UU	UU		19b. TELEPHONE NUMBER: 919-660-1526

Report Title

Final Report on "Sculpting Molecular Potentials to Design Optimized Materials: The Inverse Design of New Molecular Structures" (Agreement #W911NF0410243)

ABSTRACT

The aim of this project was to develop inverse design methods capable of designing optimized molecular species and materials. The project involved the development of continuous, integer, and hybrid molecular optimization methods that allow the identification of optimal target species. A component of this project involves the synthesis and characterization of these candidate materials. The target property in this project is the nonlinear optical response of organic species. The outcome of this project was a suite of methods useful for the design and optimization of molecular materials.

List of papers submitted or published that acknowledge ARO support during this reporting period. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

N. Jiang, G. Zuber, S. Keinan, M.J. Therein, W. Yang, D.N. Beratan, "Design of coupled porphyrin chromophores with unusually large hyperpolarizability," in preparation (2010).

D. Balamurugan, S. Keinan, W. Yang and D.N. Beratan, Inverse design of push-pull V-shaped nonlinear optical molecules with optical transparency, in preparation (2010).

X. Hu, H. Hu, D.N. Beratan and W. Yang, "A gradient-directed Monte Carlo approach for protein design," J. Comp. Chem., online (2010).

X. Hu, D. Xiao, S. Keinan, I. Asselberghs, M.J. Therien, K. Clays, W. Yang, and D.N. Beratan, "Predicting the Frequency Dispersion of Electronic Hyperpolarizabilities on the Basis of Absorption Data and Thomas-Kuhn Sum Rules," J. Phys. Chem. C, 114, 2349-2359 (2010).

X. Hu, D.N. Beratan, and W. Yang, "Emergent strategies for inverse molecular design," Science in China B: Chemistry, 52, 1769-1776 (2009).

X. Hu, D.N. Beratan, and W. Yang, "A gradient-directed Monte Caro method for global optimization in discrete space: Application to protein sequence design and folding," J. Chem. Phys., 131, 154117 (2009).

B.C. Rinderspacher, J. Andzelm, A. Rawlett, J. Dougherty, D.N. Beratan, W. Yang, "Discrete optimization of electronic hyperpolarizabilities in a chemical subspace," J. Chem. Theory Comput., 5, 3321-3329 (2009).

L. Yuan, J. Seo, N.S. Kang, S. Keinan, S.E. Steele, G.A. Michelotti, W.C. Wetsel, D.N. Beratan, Y-D. Gong, T.H. Lee and J. Hong, "Identification of 3-Hydroxy-2-(3-Hydroxyphenyl)-4H-1-Benzopyran-4-Ones as Isoform-Selective PKC-? Inhibitors and Potential Therapeutics for Psychostimulant Abuse," Mol. BioSyst., 5, 927-930 (2009).

S. Keinan, M.J. Therien, D.N. Beratan and W. Yang, "Molecular design of porphyrin based nonlinear optical materials," J. Phys. Chem. A, 112, 12203-12207 (2008).

D. Balamurugan, W. Yang, and D.N. Beratan, "Exploring chemical space with discrete, gradient and hybrid optimization methods," J. Chem. Phys., 129, 174105 (2008).

D. Xiao, W. Yang and D.N. Beratan, "Inverse molecular design in a tight-binding framework," J. Chem. Phys., 129, 044106 (2008).

X. Hu, D.N. Beratan, and W. Yang, "A gradient-directed Monte Carlo approach to molecular design," J. Chem. Phys., 129, 064102 (2008).

S. Keinan, W.D. Paquette, J.J. Skoko, D.N. Beratan, W. Yang, S. Shinde, P.A. Johnston, J.S. Lazo, and P. Wipf, "Computational design, synthesis and biological evaluation of para-quinoid-based inhibitors for redox regulation of the dual-specificity phosphatase Cdc25B," Org. Biomol. Chem., 6, 3256-3263 (2008).

D. Xiao, F. Bulat, W. Yang, D.N. Beratan, "A donor-nanotube paradigm for nonlinear optical materials," Nano Lett., 8, 2814-2818 (2008).

T. V. Duncan, K. Song, S.-T. Hung, I. Miloradovic, A. Persoons, T. Verbiest, M. J. Therien, and K. Clays, "Molecular Symmetry and Solution Phase Structure Interrogated by Hyper-Raleigh Depolarization Measurements: Insights for Elaborating Highly Hyperpolarizable D2 –Symmetric Chromophores," Angew. Chemie, Int. Ed. Engl. 2008, 47, 2978 –2981.

Number of Papers published in peer-reviewed journals: 15.00

(b) Papers published in non-peer-reviewed journals or in conference proceedings (N/A for none)

B.C. Rinderspacher, J. Andzelm, A. Rawlett, J. Dougherty, D.N. Beratan, W. Yang, "Discrete optimization of electronic hyperpolarizabilities in a chemical subspace," Army Research Laboratory Publication ARL-TR-4833, May 2009.

Number of Papers published in non peer-reviewed journals: 1.00

(c) Presentations

XIANGQIAN HU
May. 2009, Annual Meeting of Southeastern Theoretical Chemistry Association, Duke University.
Aug. 2009, ACS National Meeting, Washington, DC.
Oct. 2009, Hong Kong University.

DAVID BERATAN
University of North Carolina - Chapel Hill, 1/09

MICHAEL THERIEN
National American Chemical Society Meeting, Philadelphia, August 18th, 2008.
Department of Chemistry, University of Leuven, Leuven, BELGIUM, October 20th, 2008.
University of Hasselt, Hasselt, BELGIUM, November 6th, 2008.
University of Hasselt, Hasselt, BELGIUM, November 20th, 2008.

Number of Presentations: 8.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Number of Non Peer-Reviewed Conference Proceeding publications (other than abstracts): 0

Peer-Reviewed Conference Proceeding publications (other than abstracts):

Number of Peer-Reviewed Conference Proceeding publications (other than abstracts): 0

(d) Manuscripts

Number of Manuscripts: 0.00

Patents Submitted

"Methods and systems for selecting molecular structures," provisional patent application, submitted 2/16/07; patent filed 6/12/08.

Patents Awarded

Graduate Students

NAME	PERCENT_SUPPORTED
Nan Jiang	
Horacio Carias	
Timothy Heaton-Burgess	
Xiancheng Zeng	
Dequan Xiao	0.00
FTE Equivalent:	**0.00**
Total Number:	**5**

Names of Post Doctorates

NAME	PERCENT_SUPPORTED
Xiangqian Hu	0.34
Desinghu Balamurugan	
Paula Mori-Sanchez	0.07
Aron Cohen	
R. Christopher Rinderspacher	1.00
Shahar Keinan	1.00
Ravindra Venkatramani	
Mingliang Wang	
Inge Asselberghs	
FTE Equivalent:	**2.41**
Total Number:	**9**

Names of Faculty Supported

NAME	PERCENT_SUPPORTED	National Academy Member
David Beratan		No
Weitao Yang		No
Michael Therien		No
Donald Rose		No
Koen Clays		No
FTE Equivalent:		
Total Number:	**5**	

Names of Under Graduate students supported

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Student Metrics

This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period:	0.00
The number of undergraduates funded by this agreement who graduated during this period with a degree in science, mathematics, engineering, or technology fields:.....	0.00
The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields:.....	0.00
Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale):	0.00
Number of graduating undergraduates funded by a DoD funded Center of Excellence grant for Education, Research and Engineering:	0.00
The number of undergraduates funded by your agreement who graduated during this period and intend to work for the Department of Defense	0.00
The number of undergraduates funded by your agreement who graduated during this period and will receive scholarships or fellowships for further studies in science, mathematics, engineering or technology fields:	0.00

Names of Personnel receiving masters degrees

NAME
Total Number:

Names of personnel receiving PHDs

NAME
Dequan Xiao
Timothy Heaton-Burgess
Total Number: 2

Names of other research staff

NAME	PERCENT_SUPPORTED	
Cecilia Eichenberger	0.00	No
Michael Peterson	0.00	No
FTE Equivalent:	**0.00**	
Total Number:	**2**	

Sub Contractors (DD882)

1 a. Katholieke Universiteit Leuven 1 b. Celestijnenlaan 200F

B-3001 Leuven 00000

Sub Contractor Numbers (c):

Patent Clause Number (d-1):

Patent Date (d-2):

Work Description (e): hyper-Rayleigh scattering characterization of nonlinear optical materials

Sub Contract Award Date (f-1):

Sub Contract Est Completion Date(f-2):

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1 a. Katholieke Universiteit Leuven 1 b. Celestijnenlaan 200F

B-3001 Leuven 00000

Sub Contractor Numbers (c):

Patent Clause Number (d-1):

Patent Date (d-2):

Work Description (e): hyper-Rayleigh scattering characterization of nonlinear optical materials

Sub Contract Award Date (f-1):

Sub Contract Est Completion Date(f-2):

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1 a. University of Pennsylvania 1 b. Office of Research Services

University of Pennsylvania

Philadelphia PA 19104

Sub Contractor Numbers (c):

Patent Clause Number (d-1):

Patent Date (d-2):

Work Description (e): synthesis and characterization of nonlinear optical materials

Sub Contract Award Date (f-1):

Sub Contract Est Completion Date(f-2):

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1 a. University of Pennsylvania 1 b. Research Services

P221 Franklin Building

Philadelphia PA 191046205

Sub Contractor Numbers (c):

Patent Clause Number (d-1):

Patent Date (d-2):

Work Description (e): synthesis and characterization of nonlinear optical materials

Sub Contract Award Date (f-1):

Sub Contract Est Completion Date(f-2):

Inventions (DD882)

Statement of the problem studied.

This project, supported from 2004 to 2009, aimed at developing theoretical tools to assist in the design of real optimal molecular structures and materials. That is, the project combined state of art quantum chemical methods with newly developed approaches to property optimization in order to establish an "inverse design" framework for designing optimal molecular structures. The majority of the research was theoretical in nature and was performed at Duke University. A limited investment was made in synthetic methodology and in the development of state-of-art characterization methods (through collaborations with the Therien and Clays groups). Our targeted property was the molecular first hyperpolarizability, known as β.

Summary of the most important results and Bibliography

Our progress on the theoretical front was particularly noteworthy. In this final report, we present a chronological summary of our project, emphasizing our key developments and discoveries in the context of our published contributions:

2006

- M. Wang, X. Hu, D.N. Beratan, and W. Yang, "Designing molecules by optimizing potentials," submitted to J. Am. Chem. Soc., 128, 3228-3232 (2006).

Our first, and perhaps our key contribution, was to establish a new theoretical methodology to map the challenge of discrete chemical optimization onto a problem of continuous optimization. This was accomplished with our "linear combination of atomic potentials" (LCAP) approach, described in a 2006 *Journal of the American Chemical Society* publication. To date, this paper has been cited 37 times, and it was highlighted in numerous periodicals. This contribution defined the core continuous optimization approach used in much of the project.

2007

- S. Keinan, X. Hu, D.N. Beratan, W. Yang, "Designing molecules with optimal properties using the linear combination of atomic potentials approach in an AM1 semiempirical framework," J. Phys. Chem. A, 111, 176-181 (2007).

In 2007, we expanded the LCAP approach to semiempirical electronic structure methods, allowing the exploration of much larger molecular spaces. This paper also provided the first exploration of mixed discrete optimization methods with property gradient guided approaches.

2008

- S. Keinan, M.J. Therien, D.N. Beratan and W. Yang, "Molecular design of porphyrin based nonlinear optical materials," J. Phys. Chem. A, 112, 12203-12207 (2008).
- D. Balamurugan, W. Yang, and D.N. Beratan, "Exploring chemical space with discrete, gradient and hybrid optimization methods," J. Chem. Phys., 129, 174105 (2008).
- D. Xiao, W. Yang and D.N. Beratan, "Inverse molecular design in a tight-binding framework," J. Chem. Phys., 129, 044106 (2008).
- X. Hu, D.N. Beratan, and W. Yang, "A gradient-directed Monte Carlo approach to molecular design," J. Chem. Phys., 129, 064102 (2008).
- S. Keinan, W.D. Paquette, J.J. Skoko, D.N. Beratan, W. Yang, S. Shinde, P.A. Johnston, J.S. Lazo, and P. Wipf, "Computational design, synthesis and biological evaluation of

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- D. Xiao, F. Bulat, W. Yang, D.N. Beratan, "A donor-nanotube paradigm for nonlinear optical materials," Nano Lett., 8, 2814-2818 (2008).
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2008 saw a considerable expansion of our optimization approach into property gradient biased Monte Carlo methods, providing a marriage between our continuous (property derivative LCAP) methods and discrete optimization. We also provided quantitative benchmarks among discrete, continuous, and hybrid optimization methods in 2008. This year also saw the synthetic program come on line, and we began to perform the optimization of realistic families of nonlinear optical chromophores that were found to have predicted order of magnitude property enhancements compared to prior benchmark structures. We also showed that our methods could explore molecular spaces of astronomical size when the chemical species are closely related structurally.

2009

- X. Hu, D.N. Beratan, and W. Yang, "Emergent strategies for inverse molecular design," Science in China B: Chemistry, 52, 1769-1776 (2009).
- X. Hu, D.N. Beratan, and W. Yang, "A gradient-directed Monte Caro method for global optimization in discrete space: Application to protein sequence design and folding," J. Chem. Phys., 131, 154117 (2009).
- B.C. Rinderspacher, J. Andzelm, A. Rawlett, J. Dougherty, D.N. Beratan, W. Yang, "Discrete optimization of electronic hyperpolarizabilities in a chemical subspace," J. Chem. Theory Comput., 5, 3321-3329 (2009).

2009 saw continued development of gradient-guided Monte Carlo optimization approaches, broadening the applicability of our methodology.

2010

- N. Jiang, G. Zuber, S. Keinan, M.J. Therein, W. Yang, D.N. Beratan, "Design of coupled porphyrin chromophores with unusually large hyperpolarizability," in preparation (2010).
- D. Balamurugan, S. Keinan, W. Yang and D.N. Beratan, Inverse design of push-pull V-shaped nonlinear optical molecules with optical transparency, in preparation (2010).
- X. Hu, H. Hu, D.N. Beratan and W. Yang, "A gradient-directed Monte Carlo approach for protein design," J. Comp. Chem., online (2010).
- X. Hu, D. Xiao, S. Keinan, I. Asselberghs, M.J. Therien, K. Clays, W. Yang, and D.N. Beratan, "Predicting the Frequency Dispersion of Electronic Hyperpolarizabilities on the Basis of Absorption Data and Thomas-Kuhn Sum Rules," J. Phys. Chem. C, 114, 2349-2359 (2010).

Finally, studies of 2009-10 established firm links between our optimization approach and experiment. Perhaps the most exciting development in our formalism was a Thomas-Kuhn sum

rule method that predicts the frequency dispersion of β based purely on experimental linear spectroscopy and a limited number of β values at specific frequencies. This could prove a breakthrough, as chromophore design will be of the greatest utility when it can address design as specific telecom wavelengths. In addition, we performed molecular optimization in specific rich "structural subspaces" that can be accessed by our experimental collaborators. Indeed, the predicted structures discovered in the computations are expected to produce order of magnitude enhancements of molecular hyperpolarizabilities above those accessible in currently existing structures.